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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,980	04/24/2006	Edwin Andries Gerard Van Der Vossen	1347700002US	4140

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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,980	VAN DER VOSSEN ET AL.	
	Examiner	Art Unit	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-32 and 34-46* is/are pending in the application.

4a) Of the above claim(s) *8-32,34-38 and 40-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,39 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's cancellation of claim 2, amendments to claims 1, 4-8, and 39, as well as submission of new claims 44-46 filed on 10/24/2007 are acknowledged.

As a result, claims 1, 3-32 and 34-46 are pending.

Claims 8-32, 34-38 and 40-43 are withdrawn for being drawn to non-elected inventions.

Claims 1, 3-7, 39 and 44-46 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The objections to the specification are withdrawn in light of Applicants' amendments and argument.

4. All the rejections to claim 2 are withdrawn due to the cancellation of the claim.

5. The rejections of claims under U.S.C 102 (b) and 102 (b)/103(a) are withdrawn due to claim amendment.

6. The rejection of claims under U.S.C 103(a) is withdrawn due to claim amendment.

Claim Rejections - 35 USC § 112

7. Claims 1, 3-7, 39 remain and claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the recitation, "high stringency conditions", in part (d) renders the claim indefinite. The term, "stringent" is a relative term with no definite meaning. It is unclear what is considered to a stringent condition. The metes and bounds are not clear.

8. Claims 1, 3-7, 39 remain and claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed April 24, 2007. Applicants traverse in the paper filed October 24, 2007. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that claim 1 has been amended to recite the Rpi-blb2 protein encoding nucleic acid comprising the nucleotide sequences of SEQ ID NO: 1, 3, 5 and 6 and the nucleotide sequences encoding proteins at least 82% identical to SEQ ID NO: 2 or 4 (response, page 16, 1st paragraph) and that the specification describes four nucleic acid molecules, SEQ ID NO: 1, 3, 5, and 6, which encode the protein of SEQ ID NO: 2 or 4 with anti-Oomycete activity (response, page 16, 2nd paragraph). However, SEQ ID NO: 1, 3, 5, and 6 all encode SEQ ID NO: 2 or 4, whereas the claims are broadly drawn to a genus of nucleotide sequences encoding proteins at least 82% identical to SEQ ID NO: 2 or 4. SEQ ID NO: 1, 3, 5 and 6 are not considered as a representative number of species within the claimed genus.

Applicants further argue that the specification provides conserved domains of the Rpi-blb2 proteins include LZ, NBS and LRR domains (response, page16, the 3rd paragraph). However, the motifs of NBS and LRR are obtained ONLY by alignment of genes associated with pathogen resistance genes. There is no experimental evidence shown by either the specification or prior art that NBS and LRR domains are related to the function of anti-Oomycetes activity. In addition, NBS and LRR are motifs existing in many proteins unrelated to disease resistance. Are those motifs dispensable to the anti-Oomycetes activity? What else besides those motifs might constitute essential structures for anti-Oomycetes? Thus, the specification does not describe conserved structures of SEQ ID NO: 2 or 4 that are essential to its functional activity. Without correlating the conserved structure to the function, even if it is known in the art that conservative amino acid substitutions can be made (response, the paragraph bridging

pages 17-18), a person skilled in the art still would not know which residues can be modified and to which residue such substitution can be made.

Further, without well defined "high stringent condition for hybridization ", any DNA could hybridize to the sequences of nucleotide sequences encoding SEQ ID NO: 2 or 4 more or less at an appropriate condition.

Still further, the state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40:857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotides mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment of Frourgoux-Nicol et al exhibits less than 50% sequence identity with the probe to which the fragment hybridized. In the instant case, for example, the claimed nucleotide sequences would encompass a nucleotide acid with up to 5 kb mismatches across SEQ ID NO: 6. Without further guidance, undue experimentation would be required for a person skilled

in the art to generate and verify variants of SEQ ID NO: 1, 3, 5 and 6 and still have anti-Oomycetes activity.

Furthermore, the specification does not indicate that reverse complement DNA strand of SEQ ID No. 1, 3, 5 and 6 also has anti-Oomycetes activity. A nucleotide sequence hybrizable to SEQ ID No. 1, 3, 5 and 6 is expected to be reverse complement to DNA strand of SEQ ID No. 1, 3, 5 and 6, and therefore is unlikely to have anti-Oomycetes activity.

9. Claims 1, 3-7, 39 remain and claims 44-46 are rejected under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for a method for increasing resistance of a plant to a plant pathogen of Oomycete by overexpression of a transgene encoding a Rpi-blb2 protein of SEQ ID NO: 2 or 4, does not reasonably provide enablement for nucleotide sequences encoding any Rpi-blb2 proteins, or any nucleotide sequences encoding any variant of SEQ ID NO: 2 or 4 as described in c)-d) of claim 1, or increasing activity of SEQ ID NO: 2 or 4 by others meanings including steps a)-e) of claim 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims, for the reasons of record stated in the Office action mailed April 24, 2007. Applicants traverse in the paper filed October 24, 2007. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that screening and testing for homologs or variants of Rpi-blb2 protein only require routine experiment and is not undue (response, page 17, 3rd

paragraph). The examiner disagrees. As discussed above for written description rejection, the specification does not describe conserved structures of SEQ ID NO: 2 or 4 that are essential to its functional activity. Without correlating the conserved structure to the function, even if it is known in the art that conservative amino acid substitutions can be made (the paragraph bridging pages 17-18), a person skilled in the art still would not know which residues can be modified and to which residue such substitution can be made. Therefore, without further guidance, to generate claimed genus of sequences is undue. For example, the sequence of SEQ ID NO: 2 consists of 1267 residues. A polypeptide having 82% identity to it differs in any over 220 residues. One skilled in the art would not just randomly change any 176 residues of SEQ ID NO: 2 or 4, by any type of addition, substitution, and/or deletion, to obtain a sequence that differs by 18%. One requires further guidance regarding the regions of SEQ ID NO: 2 or 4 that can tolerate change, and one requires guidance regarding the type of change that would be. The specification provides no guidance in that regard. Furthermore, Lazar et al. and Hill et al teach that making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results (previous office action, page 12, 2nd paragraph).

Finally, increasing the activity of Rpi-blb2 protein can be achieved in many ways including the meanings listed in steps a)-g) of claim6. However, the specification only teaches how to practice the invention by expressing anti-Oomycete protein of SEQ ID NO: 2 as a transgene in transgenic plant. The specification is silent as to how to use other methods to increase the activity of Rpi-blb2 protein. For example, the specification

does not provide guidance on which genes are involved in up-regulating the expression of Rpi-blb2 protein (part (d) of claim 6), what exogenous inducing factors are (part (e) of claim 6), how to increasing specific activity/stability of the Rpi-blb2 protein (part (a) and (c) of claim 6), or how to stabilize the mRNA encoding resistance gene (part (b) of claim 6). Undue experimentation would be required to practice the invention using ways other than transgenically expressing Rpi-blb2 protein (previous office action, page 15, 1st paragraph). Applicants fail to respond the rejection in this regard.

Summary

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ELIZABETH MCELWAIN
PRIMARY EXAMINER